

REMARKS

Upon amendment, Claims 1-5, 10, 12-16, and 52 are pending in this application. Claims 1, 3, 10, 12, 14, 15, 16, and 52 have been amended.

Claims 1 and 52 have been amended to recite that the method claimed is for isolating a non-proteinaceous small molecule for further characterization. Claims 3 and 10 have been amended to correct the claim dependencies. Claims 12, 14, 15, and 16 have been amended to recite the techniques for further characterization. Support for this amendment can be found throughout the Specification as originally filed; in particular, at least, for example, in original Claim 11 and at Page 4, line 31 to Page 5, line 5. No new matter has been added.

Amendment of the Claims is not to be construed as acquiescence to any objections/rejections set forth in the pending Office Action, or any previous Office Action, and was done solely to expedite prosecution of the Application. Applicants respectfully reserve the right to pursue any non-elected, canceled, or otherwise unclaimed subject matter in one or more continuation, continuation-in-part, or divisional applications.

Rejections under 35 U.S.C. § 103(a)

Claims 1, 3-16, and 52 are rejected under 35 U.S.C. 103 (a), as unpatentable over the combination of PCT International Patent Publication No. WO 00/70334A1 to Lee ("Lee") in view of United States Published Patent Application No. US 2005/0153346 to Schneider ("Schneider"). Applicants respectfully disagree and traverse the rejection.

Claim 1 recites a method for isolating a non-proteinaceous small molecule for further characterization comprising contacting a biological sample; said sample containing at least one non-proteinaceous small molecule with a surfactant wherein the isolation comprises dissociation of a non-proteinaceous small molecule from a biological sample and wherein the non-proteinaceous small molecule is not a peptide. As discussed in prior responses, Lee describes the analysis of large molecules, *specifically proteins or peptides*. The Examiner alleges that Lee, in teaching the potential use of MALDI, shows that is desirable to use the elected surfactant to improve the analysis of "digests" and equates the presumed "digests" of Lee with non-proteinaceous small molecules.

Indeed, as discussed in the interview, Lee is focused primarily on the analysis of entire proteins. As such, Applicants contend that nothing in Lee teaches or suggests the analysis of

non-proteinaceous small molecules which are isolated from a biological sample. Even if one were to read the digestion of Lee as teaching non-proteinaceous small molecules, one of ordinary skill in the art would not readily consider such digestion as dissociating a small molecule contained within the sample but merely the creation of a new small molecule as a byproduct of the digestion of the large molecules of the sample. That is to say, **there is no teaching or suggestion in Lee of the dissociation of a non-proteinaceous small molecule from the protein binding effect of a biological sample.**

Schneider does nothing to rectify the deficiencies of Lee. Schneider merely describes the use of MALDI for the analysis of different sized molecules. Indeed, a careful reading of Schneider would lead one of ordinary skill in the art away from the Examiner's assertion that MALDI analysis would digest large molecules into small molecules as Schneider states that MALDI is one of "the best able to *ionize large, low volatility molecular species.*" (See, Paragraph 125, emphasis added). As such, even if one of ordinary skill were to look to Schneider for the teaching that MALDI can be used for non-proteinaceous small molecular species, the same artisan would have been taught that *proteinaceous large molecules are ionized* by MALDI and not digested into non-proteinaceous small molecular species. Again, even if one were to read Schneider to include the digestion of proteinaceous large molecules, at best, one of ordinary skill in the art would not readily consider such digestion as dissociating a small molecule contained within the sample but merely the creation of a new small molecule as a byproduct of the digestion of the large molecules of the sample. **There is no teaching or suggestion in Schneider of the dissociation of a non-proteinaceous small molecule from the protein binding effect of a biological sample.**

Even if one of ordinary skill in the art were motivated to combine the references, Applicants respectfully submit that he would have lacked the necessary expectation of success in utilizing a surfactant as described by Lee for the isolation of one or more non-proteinaceous small molecules contained within a biological sample such that the small molecule is dissociated from the biological sample. At best, one of ordinary skill in the art may have expected the surfactant to assist in the analysis of proteins or peptides which make up the biological sample or produced by digestion of the biological sample itself, as surfactants have historically been used only for the analysis of similar large molecules due to their binding characteristics. (See background section of Application.)

Finally, as previously argued and discussed above, the effect of the use of the surfactant disclosed in the present invention has a surprising and unexpected result of releasing a small molecule from a biological sample for isolation and further characterization. In particular, the surfactants provided by the present invention surprisingly and unexpectedly avoid the protein binding of small molecules in a biological sample associated with other surfactants such as SDS. As a result of this invention, near complete recovery of a small molecule in a biological sample can be obtained without further ion suppression upon analysis thereby allowing for determination of small molecule in a sample in total, free form and bound form. See, for example, Comparative Example 2 and the data presented in Figure 1.

Assuming for the sake of argument that the Office Action has made out a *prima facie* showing of obviousness based on the cited combination of records, M.P.E.P. §2144.05 indicates that “[a] *prima facie* case of obviousness may also be rebutted by showing that the art, in any material respect, teaches away from the claimed invention. *In re Geisler*, 116 F.3d 1465, 1471, 43 USPQ2d 1362, 1366 (Fed. Cir. 1997)”. In view of the unexpected and surprising result afforded by the claimed invention, Applicants have rebutted any *prima facie* showing of obviousness if such a showing had been made.

Accordingly, Applicants respectfully request reconsideration and withdrawal of all rejections under 35 U.S.C. § 103 of Claims 1-16 and 52.

Double Patenting rejections

Claims 1, 3-16, and 52 are provisionally rejected on the grounds of non-statutory obviousness-type double patenting over Claims 1, 3-5, 7-9, 11, 13-18, 20-30, 33, and 123 of U.S. Patent Application Serial No. 10/516,418. Similarly, Claims 1-16 and 52 are rejected on the grounds of nonstatutory obviousness-type double-patenting over Claims 1-7 and 13-20 of U.S. Patent No. 7,229,539.

As the pending claims have not yet been deemed allowable, any statement regarding the double patenting rejection made would be premature. Therefore, Applicants respectfully traverse this rejection and request that this rejection be held in abeyance until claimed subject matter is deemed allowable but for the obviousness-type double patenting rejection.

CONCLUSION

In view of the remarks made herein, Applicants submit that the application is in condition for allowance, and respectfully request favorable reconsideration of the application and prompt issuance of a Notice of Allowance are respectfully requested. If a telephone conference with Applicant's representative would be helpful in resolving any remaining issues and/or expediting prosecution of the application, Applicants invite the Examiner to contact the undersigned at the telephone number indicated below before issuance of the next office action. Applicants thank the Examiner in advance for this courtesy.

Applicants believe that no additional fees are required in connection with this paper, other than the fee for the extension of time. Nevertheless, Applicants authorize the Director to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to Deposit Account No. 04-1105, under Order No. 60008US(49991).

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Respectfully submitted,

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